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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	Rothschild, et al.
SERIAL NO	:	09/380,419
FILED	:	July, 24, 2000
TITLE	:	MELANOCORTIN-4 RECEPTOR GENE AND USE AS A GENETIC MARKER FOR FAT CONTENT, WEIGHT GAIN, AND/OR FEED CONSUMPTION OF ANIMALS
Grp./A.U.	:	1655
Examiner	:	Einsmann, J.
Conf. No.	:	2593
Docket No.	:	P0381US1

AMENDMENT AFTER FINAL REJECTION

Assistant Commissioner for Patents
Washington, D.C. 20231

Madam:

It is respectfully requested that this Amendment After Final Rejection be entered and made of record. It is believed that the following amendments and remarks place the application in the form for allowance. The following amendments and remarks at least place the claims in a better form for appeal. No new matter is presented, as such the amendment is proper under 37 C.F.R. § 1.116. Applicants respectfully request reconsideration.

FACSIMILE TRANSMISSION (37 C.F.R. § 1.6(a)(3))

I hereby certify that this document and the documents referred to as enclosed therein are being transmitted via facsimile to Technology Center 1600 (Art Unit 1655) 703-872-9307, Attn: Assistant Commissioner for Patents, Washington, D.C. 20231, on this 21 day of March, 2002.

Heidi S. Nebel

In the Specification

Please amend the specification as follows:

On page 5, line 2, please delete "(SEQ ID NO: 3)" and insert--(SEQ ID NO: 1)--.

On page 5, line 4, please delete "(SEQ ID NO: 4)" and insert--(SEQ ID NO: 3)--.

On page 5, line 6, please delete "(SEQ ID NO: 12)" and insert--(SEQ ID NO: 11)--.

On page 5, line 13 please insert after the word MC4R--SEQ ID NO: 11--.

On page 5, line 14, please insert after P32245--(SEQ ID NO: 12)--.

On page 5, line 14, please insert after P70596--(SEQ ID NO: 13)--.

On page 5, line 14, please insert after P41983--(SEQ ID NO: 14)--.

On page 5, line 14, please insert after P56451--(SEQ ID NO: 15)--.

On page 5, line 15, please insert after P34974--(SEQ ID NO: 16)--.

On page 5, line 15, please insert after P41968--(SEQ ID NO: 17)--.

On page 5, line 15, please insert after P33033--(SEQ ID NO: 18)--.

On page 5, line 15, please insert after Q01718--(SEQ ID NO: 19)--.

On page 5, line 15, please insert after Q01726--(SEQ ID NO: 20)--.

On page 5, line 15, please insert after Q28031--(SEQ ID NO: 21)--.

On page 5, line 15, please insert after AF011466--(SEQ ID NO: 22)--.

On page 5, line 15, please insert after P21554--(SEQ ID NO: 23)--.

On page 5, line 15, please insert after P18089--(SEQ ID NO: 24)--.

On page 5, line 16, please insert after P30680--(SEQ ID NO: 25)--.

On page 5, line 16, please insert after P47211--(SEQ ID NO: 26)--.

On page 6, line 29, please delete "SEQ ID NO: 8" and insert--SEQ ID NO: 7--.

On page 6, line 29, please delete "SEQ ID NO: 9" and insert--SEQ ID NO: 8--.

On page 7, line 25, please delete "(SEQ ID NO: 6)" and insert--(SEQ ID NO: 5)--.

On page 7, line 26, please delete "(SEQ ID NO: 7)" and insert--(SEQ ID NO: 6)--.

On page 7, line 27, please delete "(SEQ ID NO: 8)" and insert--(SEQ ID NO: 7)--.

On page 7, line 28, please delete "(SEQ ID NO: 9)" and insert--(SEQ ID NO: 8)--.

On page 8, line 14, please delete "Taqman™" and insert--TAQMAN™--.

On page 10, line 5, please delete "(SEQ ID NO: 6)" and insert--(SEQ ID NO: 5)--.

On page 10, line 6, please delete "(SEQ ID NO: 7)" and insert—(SEQ ID NO: 6)--.

On page 11, line 28, please delete "(SEQ ID NOS: 2-5)" and insert--(SEQ ID NOS: 2-4)--.

On page 12, line 20, please delete "(SEQ ID NO: 8)" and insert--(SEQ ID NO: 7)--.

On page 12, line 21, please delete "(SEQ ID NO: 9)" and insert--(SEQ ID NO: 8)--.

On page 19, line 17, please delete "(SEQ ID NO: 6)" and insert--(SEQ ID NO: 5)--.

On page 19, line 18, please delete "(SEQ ID NO: 7)" and insert--(SEQ ID NO: 6)--.

On page 20, line 1, please delete "(SEQ ID NO: 10)" and insert--(SEQ ID NO: 9)--.

On page 20, line 2, please delete "(SEQ ID NO: 11)" and insert--(SEQ ID NO: 10)--.

In the Claims

Please amend the following claims:

1.(Twice Amended)

A method of identifying an animal which possesses a genotype associated with variation in one or more favorable metabolic traits selected from fat content, growth rate, and feed consumption, the method comprising:

obtaining a nucleic acid sample from the animal; and

assaying for the presence of a polymorphism in the MC4R gene associated with variation in one or more of the metabolic traits of fat content, growth rate, and feed consumption.

2.(Twice Amended)

The method of claim 1 wherein the polymorphism is identified at position 678 of a PCR sequence of the MC4R gene in pigs and other animals.

4. (Twice Amended)

The method of claim 2 wherein the polymorphism is a guanine at base 678 in a PCR sequence of the MC4R gene associated with variation in fat content.

5. (Twice Amended)

The method of claim 2 wherein a marker for lower feed intake, than animals without the marker, is identified by an adenine at base 678 of a PCR sequence of the MC4R gene.

6. (Twice Amended)

The method of claim 2 wherein a marker for faster rate of gain, than animals without the marker, is identified by an adenine at base 678 of a PCR sequence of the MC4R gene.

10. (Twice Amended)

The method of claim 1 further comprising the step of amplifying polymorphism in the MC4R gene sequence with primers.

20. (Twice Amended)

A method of identifying an animal which possess a desired genotype associated with variation in one or more metabolic traits selected from fat content, growth rate, and feed consumption, the method comprising:

obtaining a nucleic acid sample from an animal;

amplifying nucleic acid of said sample with primers SEQ ID NO: 5 and SEQ ID NO: 6.

sequencing the amplified product to reveal a nucleotide substitution within a *Taq I* restriction enzyme recognition site;

digesting the amplified product with *Taq I* to obtain fragments;

separating the fragments obtained from the digestion, and

generating a MC4R gene fragment having one *Taq I* restriction site with primers SEQ ID NO: 9 and SEQ ID NO: 10; and

identifying the presence or absence of a *Taq I* site

wherein the presence of a *Taq I* restriction site identifies the presence of a polymorphic site in the MC4R gene associated with variation in one or more of the metabolic traits in the animal.

22. (Amended)

The method of claim 20 wherein the site is identifiable by fragments of 466, 225, and 76 bp when a guanine is present at base 678 of the amplified product and fragments of 542 and 225 bp when an adenine is present when a restriction enzyme which cuts at the same recognition site as *Taq I* is used.

23. (Twice Amended)

The method of claim 20 wherein the step of identifying comprises detecting a *Taq I* restriction pattern.

28. (Twice Amended)

A method for selecting animals possessing a desired pair of alleles associated with variation in one or more favorable metabolic traits selected from lower fat content, faster growth rate, or lower feed consumption, than animals without said alleles, comprising:

obtaining a nucleic acid sample from an animal;

identifying the alleles associated with a desired metabolic trait, and

selecting the animals which have desired alleles.

29. (Twice Amended)

A method for an indirect selection of a polymorphism in a MC4R gene associated with variation in one or more metabolic traits selected from fat content, growth rate, and feed consumption comprising:

selecting specific alleles of an alternative DNA marker associated with the MC4R gene, wherein the MC4R gene is associated with a particular metabolic trait;

making an indirect selection of the polymorphism; and

establishing a linkage between the specific alleles of the alternative DNA and alleles of the DNA marker associated with the metabolic trait .

31. (Twice Amended)

A method of identifying animals to determine the association between a pair of alleles and one or more metabolic traits of interest selected from fat content, growth rate, and feed consumption, the method comprising:

obtaining a sample of animals from a line or breed of interest,

preparing genomic DNA from each animal in the sample,

determining the alleles present, and

calculating the association between the alleles and the trait.

32. (Twice Amended)

A method of selecting animals which possess a desired MC4R genotype associated with variation in one or more metabolic traits selected from fat content, growth rate, and feed consumption, the method comprising:

obtaining a nucleic acid sample from an animal;

identifying the genotype of the MC4R gene of the animal; and

selecting those animals which have the genotype associated with the desired traits.

33. (Amended)

A method of identifying an animal which possesses a desired polymorphism within the melanocortin-4 receptor protein of the seventh transmembrane domain at amino acid 298 comprising:

obtaining a nucleic acid sample from an animal; and

identifying the polymorphism in the translated MC4R gene

wherein an aspartic acid at amino acid 298 identifies leanness and lower feed intake, than animals without the polymorphism and an asparagine at amino acid 298 identifies a faster rate of gain than animals without the polymorphism.

REMARKS

I. Sequence Rules

Pursuant to 37 CFR 1.821 (b),which states in part: "It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier (SEQ ID NO: X) must be used, either in the drawing or in the Brief Description of the Drawings." Thus, for Fig.7, Applicants have inserted the sequence identifier in the "Brief Description of the Drawing," thus alleviating this rejection.

The amendments to the sequence identifiers in the specification will enable the sequence identifiers to match up with the Sequence Listing.

More over pursuant to 37 CFR 1.821 (b), as recited above, Applicants have shown the sequence identifier in the "Brief Description of the Drawings," (See page 5, line 6) therefore, the sequence recited in Fig. 5 does not have to be identified with a proper sequence identifier.

II. 35 USC Section § 112

Claims 1-12, 20-23, and 28-33 were rejected under 35 USC § 112, first paragraph, because the specification, while being enabling for methods of identifying the pig which possesses a genotype indicative of the pig having less back fat than pigs with a different genotype, indicative of the pig having a lower daily gain than pigs with a different genotype, or of the pig having a lower feed intake than a pig with a different genotype, wherein said method comprises screening DNA of the pig for a G to A point mutation at position 678 of SEQ ID NO: 1 (of the sequence listing) and wherein the preface of the mutation is indicative of a pig having the recitated traits, does not reasonably provide enablement for methods which screen other

animals or methods which utilize other polymorphisms. The Examiner states the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Examiner further states that the specification provides a single working example which demonstrates that in pigs homozygous for a G at position 678 of SEQ ID NO:1 is correlated with the pigs that have less back fat, lower daily gain, and lower feed take than pigs homozygous for an A at position 678. The prior art is silent with respect to other possible polymorphisms in the MC4R gene or with respect to the association of this particular polymorphism with any metabolic trait in any other animal. Neither the specification nor the prior art provide evidence of any universal correlation between polymorphisms in MC4R and metabolic traits in any other animal. With respect to other possible polymorphisms in the MC4R gene, Applicants have amended the claims to recite the MC4R polymorphism disclosed in the instant specification.

With respect to the association of this particular polymorphism with metabolic traits in any other animal, Applicants respectively traverse this rejection. Applicants have shown that polymorphism in the MC4R gene has been located and is associated with the metabolic traits of fat content, growth rate, and feed consumption in animals. Additionally, Applicants have shown that this particular polymorphism is within a highly conserved region among melanocortin receptors (MCR). Moreover, the specification discloses a multiple alignment of the predicted amino acid sequences of the pig MC4R with the MC4R protein from other species. This

alignment shows that the aspartic acid found a position 298 of the seventh transmembrane domain is very highly conserved in the MC4R protein among species.

Also, Applicants have shown that the MC4R gene consists of approximately a 1kb coding sequence contained within a single exon with the pig MC4R gene fragment being nearly the entire gene. More specifically, Applicants have shown that the marker for this metabolic trait observed in the specification is allele 1 and allele 2. Because of the evolutionary link between pigs and other species, it can be predicted that variation in this gene is also likely to be associated with the same metabolic traits in these other species. This polymorphism can be identified in the MC4R gene of these other species using the same approach set out in the specification with the resulting single nucleotide polymorphism used for association analysis.

The Examiner further states that the art is highly unpredictable with regard to the presence and functionality of polymorphic sites and genomic DNA. The amount of direction or guidance presented in the specification and the prior art of only one point mutation in the MC4R gene of one species of animal is minimal, given that just the redundancy of the genetic code would allow for several thousand different sequences when conserved or non-conserved mutations were considered, millions of different sequences for the pig MC4R gene may exist which may, or may not, have substantial differences or association with the traits interest herein. There are no working examples of additional sequences other than those disclosed in either the specification or the prior art. Applicants have amended the claims to include the specific polymorphism disclosed in the instant specification, thus alleviating this rejection.

Next, the Examiner states there is no evidence in the specification providing that the identified polymorphism is causative of the observed traits. The Examiner further states that this is a significant absence of evidence, since it is possible that the polymorphism is merely a marker for the causative genotype. The Examiner asserts that in light of the fact that the causative genotype has not been identified, it is unpredictable as to whether or not markers which are linked to the instantly disclosed polymorphism would be informative for the traits of interest herein. Applicants respectively traverse this rejection. "Although the inventor must teach how to obtain the claimed result, the inventor need not disclose or explain how or why the invention works." Fromson v. Advance offset Plate, Inc., 720 F. 2d 1565, 219 USPQ 1137 (Fed Cir. 1983). Applicants have shown that the identified polymorphism in the MC4R gene is indicative of one or more of the traits of fat content, growth rate, and feed consumption. Thus, Applicants need not understand or disclose how the polymorphism works or how it causes these metabolic traits. Therefore, Applicants respectfully request the Examiner to withdrawal this rejection.

The Examiner states that although the level of skill in the art of nucleic acid analysis is high, the quantity of the experimentation that would be necessary to determine even one additional polymorphism in the pig MC4R gene is substantial since there is no predictability for which sequences exist which code for polymorphisms in pig MC4R genes. The Examiner goes on to state the Applicants have not disclosed how one would go about detecting additional polymorphisms associated with the traits of interest herein. Because there is no reason to expect that any additional polymorphism is associated with the instantly discussed metabolic traits and because of the very large number of possible polymorphisms, screening for additional polymorphisms that would be indicators of these traits would require the rearing and subsequent

slaughtering of many, many pigs in order to analyze their metabolic traits and in order to screen the MC4R gene for informative polymorphisms. The Examiner asserts there is no evidence, however, of any frequency of significant polymorphisms. Further, even if polymorphims were detected, the polymorphism may not correlate to polymorphic traits. The instantly disclosed polymorphism may be coincident with and unrelated to a different, unlinked (on the chromosome) polymorphism such as another MC4R polymorphism or a polymorphism in an undetermined gene that actually determines the metabolic traits. The instantly disclosed polymorphism would not have any meaning or effect, but might appear to influence metabolic traits due to it's close proximity to some other gene. Applicants have amended the claims to recite only the polymorphism disclosed in the specification associated with the metabolic traits and not any other polymorphisms within the MC4R gene, thus alleviating this rejection.

The Examiner further states, the level of unpredictability and the level of experimentation required to expand the instantly disclosed methods to include animals of other species are also quite high. There is no teaching in the specification that the disclosed polymorphism even exists in animals of other species. Applicants respectfully traverse this rejection. As stated, supra on page 6, Applicants have shown a polymorphism in the MC4R gene has been located and is associated with the metabolic traits of fat content, growth rate, and feed consumption in animals. Additionally, Applicants have shown that this particular polymorphism is within a highly conserved region among melanocortin receptors. Moreover, the specification discloses a multiple alignment of the predicted amino acid sequences of the pig MC4R with the MC4R protein from other species. This alignment shows that aspartic acid found at position 298 of the seventh transmembrane domain is very highly conserved in the MC4R protein among species.

Also, Applicants have shown that the MC4R gene consists of approximately 1 kb coding sequence contained with any single exon with the pig MC4R gene being nearly the entire gene. More specifically, Applicants have shown that the marker for these metabolic traits observed in the specification are alleles 1 and 2. Because of the evolutionary link between pigs and other species, it can be predicted that variation in this gene is also likely to be associated with the same metabolic traits in other species. This polymorphism can be identified in the MC4R gene of these other species using the same approach set out in the specification with the resulting single nucleotide polymorphism used for association analysis.

The Examiner next states that since there is not evidence that the disclosed polymorphism is causative of the trait, it is highly unpredictable as to whether the polymorphism will mark the same traits in other animals. Applicants respectfully traverse this rejection. Again, as stated supra, pursuit to Fromson, Applicants need not disclose or explain how or why the invention works. The Applicants only burden is to teach how to obtain the claim results. Fromson v. Advance Offset Plate, Inc., 720 F. 2d 1565, 219, USPQ 1137 (Fed. Cir. 1983). Applicants have shown that a polymorphism in the MC4R gene has been located and this genetic variability is associated with metabolic traits. Moreover, Applicants have shown as depicted in Fig. 7 a multiple alignment of the putative seventh transmembrane domain of porcine MC4R with other MC4R proteins from other species, this alignment has shown that the aspartic acid found at position 298 of the seventh transmembrane domain is very highly conserved in the MCR proteins. Accordingly, because of the evolutionary link between pigs and other species as shown in Fig. 7, for example, it can be predicted that variation in this gene is also likely to be associated with the metabolic traits in other species. Additionally, at the gene level, the marker for leanness

and lower feed intake is for one homozygous genotype (allele 1) and the marker for another homozygous genotype (allele 2) is for faster rate of gain. Thus, Applicants have shown that there is a conserved sequence for this region. Therefore, a polymorphism at this codon will be detectable and will likely have an effect on these traits.

The Examiner further states that in order to provide such evidence, the skilled artisan would be required to undertake extensive studies of the metabolic traits of hundreds upon hundreds of different animals of each of many different species of animals. Such experimentation would be inventive in itself. Applicants respectfully traverse this rejection. The Examiner has interpreted that experimentation needed in such a way that effectively renders it impossible to obtain the claim not only for the instant invention, but for any biological invention. This approach is clearly fallacious as explained In re Angstadt. See 537 F.2d 498, 190 USPQ 214, 218 (CCPA 1976). While In re Angstadt dealt with a chemical invention, it is an adequate legal analogy. In this case, the CCPA acknowledged that the claimed invention was unpredictable and the specification did not disclose every catalyst that would work or every catalyst that would not work. Nevertheless, they held that even in unpredictable arts, the specification need not disclose every example or species covered by a claim. Similarly, Applicants acknowledge the invention is unpredictable and the specification does not disclose every species that would or would not work. However, based on the evolutionary link and comparative genomics between pigs and other species, variation in this gene is also likely to be associated with the metabolic traits in other species, thus members of the genus will behave similarly. Thus, giving predictability and enabling one skilled in the art to practice the claimed invention. Therefore, Applicants respectfully request Examiner to withdrawal this rejection.

Moreover, the instant disclosure is enabling for other animals. The specification goes into adequate detail to apprise one skilled in the relevant art to which it pertains, or with which it is most clearly connected of identifying the existence of the polymorphism in an animal. Once knowledge of the existing polymorphism is known, it takes no more than routine screening to identify the presence of the polymorphism in another species. Moreover, a polymorphism, which is in the MC4R gene, is highly conserved among species. It is expected that the different alleles disclosed in the specification also correlate with variability in this gene in other animals. The Examiner concludes by stating that due to the broad nature of the claims, the presence of only one working example, the extreme unpredictability of polymorphisms in the art, combined with the absence of teaching in the prior art and the large quantity of experimentation necessary in the art support a conclusion that undue experimentation is required to make and use the invention as broadly claimed. Applicants have addressed this rejection elsewhere in this response. (See Supra).

III. 35 USC § 112

Claim 10 was rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed at had possession of the claimed invention. MPEP 2163.06 notes " If new matter is added to the claims, the Examiner should reject claims under 35 USC § 112, first paragraph-written description requirement. In re Rasmussen, 650 F.2d 1212, to 11 USPQ 323 (CCPA 1981)." The Examiner states in the instantly rejected claim, the new limitation of "allele specific oligonucleotide type primers" in claim 10 appears to represent new matter. No specific basis for this limitation was identified in

the specification, nor did a review of the specification by the Examiner find any basis for the limitation. The specification provides methods for PCR amplification of portions of the MC4R gene, but none of these methods appear to employ allele specific oligonucleotides. Since no basis has been identified the claims are rejected as incorporating new matter. Applicants have amended the claim by deleting the recitation "allele specific oligonucleotide primers" thus alleviating this rejection.

Claims 1-12, 20-23, and 28-33 were rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 was rejected as being indefinite over the recitation of "possesses a genotype having a genetic marker." The Examiner states it is not clear how a genotype can have a genetic marker. A genotype is defined as a particular genetic pattern as seen in the DNA of an individual. "Genotype" is usually used to refer to the particular pair of alleles that an individual possesses at a certain location in the genome. Thus, the genotype does not have the marker, but describes the alleles present at the location of the marker. The Examiner states it would be more appropriate to say that the animal possesses a particular genotype or that the animal possesses nucleic acid comprising a specific version of a marker. Claims which depend from claim 1 are indefinite for this reason as well. Applicants have amended the claim by removing the phrase "having genetic markers," thus alleviating this rejection.

Claim 1 was further rejected as being indefinite. The Examiner states that phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. Thus, it is not clear if the method is for identifying an animal

which possesses a genotype indicative of variation in fat content, in growth rate, and feed consumption, or if the method is for detecting an animal which possesses an genotype indicative of variation in any metabolic traits of which those recited are a few examples. Claims which depend from claim 1 are indefinite for this reason. Applicants have amended the claim by removing the phrase "such as" to clearly show the method is for identifying an animal which possesses a genotype indicative of variation and fat content, growth rate, and feed consumption, thus making it definite. Applicants respectfully request Examiner to withdrawal this rejection.

Claim 1 was further rejected as being indefinite. The Examiner states that steps (a) and (b) appear to conflict. Step (a) requires obtaining a nucleic acid sample, while step (b) requires identifying a polymorphism in the protein. Claims which depend from claim 1 are indefinite for this reason as well. Applicants have amended the steps to show that steps (a) and (b) pertain to nucleic acid.

Claim 1 was still rejected as being indefinite because it is not clear what the method accomplishes. The Examiner states that the method appears to be a method for identifying the animal which possesses a genotype for a marker associate with particular traits. It would seem that any animal screened for such a marker would in fact have a marker that is associated with the recited traits. The claim does not specify that a particular genotype is being identified, only that an animal which possesses a genotype is identified. The Examiner further states that every animal is going to have a genotype and thus the purpose of the claim is unclear. Claims which depend from claim 1 are indefinite for this reason as well. Claim 1 has been amended to show a method for identifying an animal with favorable metabolic traits regarding fat content, growth

rate, and feed consumption, thus making the claim definite. Applicants respectfully request Examiner to withdrawal this rejection.

Claim 2 was rejected as being indefinite because of the recitation of "is characterized by a site specific mutation at amino acid..." because it is not clear what "is characterized by" means. The Examiner states this language does not clearly define a polymorphism. Furthermore, as discussed for claim 1 above, it is not clear if this method is intended to be a method for examining a nucleic acid or a polypeptide. Claims which depend from claim 2 are indefinite for this reason as well. Claim 2 has been amended by removing the recitation "is characterized by a site specific mutation at amino acid." Also, the claim has also been amended by clearly defining the polymorphism as not being "characterized by," but being "identified by." Applicants have also amended the claim to show the method is intended to be a method for examining nucleic acid, thus making the claim definite. Applicants respectfully request Examiner to withdraw this rejection.

Claim 5 was rejected as being indefinite over the recitation "wherein marker for lower feed intake, than animals without marker, is identified by" because this language is confusing and unclear. This does not appear to be proper English and is not clear what applicant is trying to convey. Furthermore, as discussed for claim 1 above, it is not clear if this method is intended to be a method for examining a nucleic acid or a polypeptide. The Applicants have amended the claim by more clearly stating the recited phrase to remove any confusion. Furthermore, the claim has been amended to show it is intended to be a method for examining a nucleic acid.

Thus making the claim definite. Applicants respectfully request the Examiner to withdrawal this rejection.

Claim 6 was rejected as being indefinite over the recitation "wherein marker for faster rate of gain, than animals without marker, is identified by" because this language is confusing and unclear. The Examiner states it does not appear to be proper English and is not clear what applicant is trying to convey. Furthermore, the phrase "marker for faster rate of gain" lacks proper antecedent basis in the claim. Furthermore, as discussed with claim 1 above it is not clear if this method is intended to be a method for examining a nucleic acid or polypeptide. Claim 6 has been amended by more clearly reciting the phrase to remove any confusion. Furthermore, Applicants have given proper antecedent basis to the phrase "marker for faster rate of gain." Additionally, the claim has been amended to show it is intended for examining a nucleic acid.

Claims 10 and 12 were rejected as being indefinite over the recitation "allele specific oligonucleotide primers." The Examiner states allele specific primers are generally understood to be designed to that they hybridize exactly to the position of a polymorphism. The primers are designed so that in the presence of one specific allele amplification will occur and in the presence of another amplification will not occur. The primers recited in claim 12, however, are not designed to hybridize to the location of any particular polymorphism, thus, if the primers recited in claim 12 are examples of the allele specific primers recited in claim 10, then it is unclear what allele specific oligonucleotide primers actually means. Applicants have amended claim 10 by removing "allele specific oligonucleotide" thereby making the claim definite. Applicants respectfully request Examiner to withdrawal this rejection.

Claims 20-23, 29-31 and newly added claim 33 are indefinite for failing to recite a final process step which agrees back with the preamble. For example, claims 20-23 are drawn to a method of identifying and animal which possesses a genotype having a genetic marker associated with metabolic traits, yet the claims recite a final step of identifying the presence or absence of a *Taq I* site in an MC4R gene fragment. The claims do not set forth a relationship between the identifying a *Taq I* site and the identifying an animal and therefore, it is not clear whether the claims are intended to be drawn to a method for identifying an animal or a method for identifying a *Taq I* site. The Examiner further states that claim 20 does not set forth any specific desired genotypes or how these are identified. Independent claims 29 and 33 have similar problems in that they also recite preambles which are not clearly met by the positive process steps of the claims. Applicants have amended claims 20-23, 29-31 and 33 by reciting a final process which agrees back with the preamble. Claim 20 has been further amended by showing how the desired genotype is identified. Applicants respectfully request Examiner to look to claim 22 to show the desired genotypes. Additionally, Applicants have amended claims 29 and 23 by reciting a preamble that meets the positive causes of process steps of the claims. Applicants respectfully request Examiner to withdrawal this rejection.

Claim 20 was rejected as being indefinite over the recitation "possesses a genotype having a genetic marker" because it is not clear how a genotype can have a genetic marker. The Examiner states, a genotype is defined as a particular genetic pattern seen in the DNA of an individual. "Genotype" is usually used to refer to the particular pair of alleles that an individual possesses at a certain location in the genome. Thus, the genotype does not have a marker, but

describes the allele present at the location of the marker. The Examiner suggests it would be more appropriate to say that the animal possesses a particular genotype or that the animal possesses nucleic acid comprising a specific version of a marker. Claims which depend from claim 20 are also indefinite for this reason as well. The Examiner further states that claims 31 and 32 recite this same problematic language. Claims 20, 31, and 32 have been amended by removing the problematic language "having a genetic marker," thus making the claim definite. Applicants respectfully request Examiner to withdrawal this rejection.

Claim 22 was rejected as being indefinite over the recitation of "at base 678" because the claim does not clearly support what base 678 is referring to. Applicants have amended the claim by clearly setting forth what base 678 is referring to.

The Examiner further states that in line 2 of Claim 20, the phrase "restriction pattern" lacks specific antecedent basis in the claim. The claim previously recites separating digestive nucleic acid fragments, but does not specifically recite a restriction pattern. Applicants believe the Examiner in making this rejection has inadvertently referred to claim 20. Applicants believe the Examiner intended to refer to claim 23. Therefore, Applicants have amended claim 23 by giving proper antecedent basis to the phrase "restriction pattern," thus making the claim definite. Applicants respectfully request the Examiner to withdrawal this rejection.

The Examiner states that claim 28 is unclear because it recites "a desired polymorphic traits" and thus, it is not clear if one or multiple polymorphic traits are being referenced. Claim 28 has been amended to show that only one polymorphic trait has been referenced.

Claim 28 was rejected as being indefinite because it appears to contradict the teachings of the specification. The Examiner states that the specification at page 7, indicates the animals homozygous for allele 1 (that is a G at position 678 of SEQ ID NO: 1) have lower fat content, and lower feed consumption, and animals homozygous for allele 2 (and A at position 678 of SEQ ID NO: 1) have a faster rate of weight gain. Yet the instant claim states that to identify animals with lower fat content, faster growth rate, or lower feed content, one must identify substitution of guanine to adenine (i.e., an "A" at position 678 of SEQ ID NO: 1). This conflicts with the specifications teaching about the allele that would indicate a faster growth rate. Clarification is required. Applicants have amended the claim by rewording, to provide clarification. These amendments are believed to make the claim definite, therefore, Applicants respectfully request Examiner to withdraw this rejection.

Next, the Examiner states that in claims 31 and 32, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claim limitation. Thus, it is not clear if the method is for identifying an animal which possesses a genotype indicative of variation in fat content, growth rate, and feed consumption, or if the method is for detecting an animal which possesses a genotype indicative of variation in any metabolic trait of which those recited are a few examples. Claims 31 and 32 have been amended to show the method for identifying an animal which possesses a genotype indicative of variation and fat content, growth rate, and feed consumption, thus making the claim definite. Applicants respectfully request Examiner to withdrawal this rejection.

Claim 31 was further rejected as being indefinite. The Examiner states the claim appears to recite two different purposes for the method in the preamble of the claim. The claim begins by reciting a method is for identifying animals which have a desired genotype, but the claim never clearly sets forth a method for identifying such animals. The claims do not provide the desired genotypes to be identified or any guidance as to how to identify which genotypes are "desire." The claim recites a step of determining an association, but the claim does not clearly set forth how the identification of animals is related to the determination of an association. Claim 31 has been amended to recite one purpose, which is a method in identifying animals to determine the association between a pair of alleles and one or more of the metabolic traits of interest, thus making the claim definite. Applicants respectfully request Examiner to withdrawal this rejection.

Claim 33 was rejected as being indefinite. The Examiner states it is not clear how identifying a polymorphism in step (d) is related to identifying an animal which possesses a desired polymorphism as recited in the preamble. Furthermore, the language of step (d) is confusing because it is not clear how to identify a polymorphism "by a nucleotide substitution." It is not clear if applicant intends to recite that a polymorphism is identified by identifying a nucleotide substitution, or some other process step. Applicants believe the Examiner has inadvertently referred to step (b) as (d) in claim 33. Applicants have amended the claim by showing how identifying the polymorphism in step (b) is related to the preamble. Furthermore, claim 33 has been amended to clearly show how to identify the polymorphism, thus making the claim definite. Applicants respectfully request Examiner to withdrawal this rejection.

IV. Conclusion

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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